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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/537,710	03/30/2000	Anders Dahlqvist	3377/99-Util	9098

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EXAMINER	
ROBINSON, HOPE A	

ART UNIT	PAPER NUMBER
1656	

DATE MAILED: 12/01/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/537,710	DAHLQVIST ET AL.	
	Examiner	Art Unit	
	Hope A. Robinson	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 September 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *30-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *30-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *7/27/04;4/5/04* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Application Status

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on September 6, 2005 has been entered.

Priority

2. As previously noted, the instant application is granted the benefit of priority for the foreign application 99106656.4 filed in Europe on April 1, 1999.

Claim Disposition

3. Claims 1-29 and 33-35 have been cancelled. Claims 30-32 have been amended. Claims 30-32 are pending and are under examination.

4. The amendment filed on September 6, 2005 has been received and entered. The amendment is improper as the claim set presented does not list all claims throughout the prosecution history. The examiner has provided that record above, however, applicant is required to submit all amendments showing the status of each claim to avoid receiving a non-responsive communication.

Maintained- Objections to the Specification

5. The specification remains objected to because of the following informalities:

(a) Previous objection to the specification for lacking complete continuity data in the first paragraph is maintained. The record indicates that the present application "claims benefit to U.S. provisional applications 60/180,687 filed February 7, 2000, 60/132,010 filed April 30, 1999 which is a continuation of U.S. Serial No. 09/329,802, filed June 10, 1999, now abandoned and claims foreign priority to EP 99106656.4, filed April 1, 1999". This information has to appear on the first page on the specification.

(b) Previous objection to the Abstract for not completely describing the disclosed subject matter is maintained. The abstract is crucial in defining the disclosed subject matter, thus, its completeness is essential. It is suggested that the abstract is amended to include the full name of the enzyme, phospholipids: diacylglycerol acyltransferase and the source species, *S. cerevisiae, S. pombe, A. thaliana, N. crassa, Z. mays,* and *L. esculentum*, for completeness.

(c) Previous objection to the specification for being confusing in amendments is maintained. The inconsistencies in the specification are summarized as follows:

(A) In an amendment filed on July 15, 2003 (Paper No. 26), the amendment to page 4 describes SEQ ID NO:18 (in its first occurrence), "Further, enzymes designated a sPDAT comprising an amino acid sequence selected from the group consisting of sequences as set forth in SEQ ID NO:16, 17 and 18 are contemplated within the scope of the invention". However, SEQ ID NO:18 is a DNA sequence.

(B) In an amendment filed on July 15, 2003 (Paper No. 26), the amendment to page 21, 3rd line, notes a correlation, "Further provisional and/or partial sequences are given as SEQ

ID NO:16 through 19, respectively", however, the nature of this respective correlation is wholly unclear.

(C) In an amendment filed on July 15, 2003 (Paper No. 26), the amendment to page 21, last line, notes SEQ ID NO:12 is an amino acid, "Excluding this nucleotide would give the amino acid sequence depicted in SEQ ID NO:12", however, this is incorrect since SEQ ID NO:12 is an *L. esculentum*, DNA sequence.

(d) Previous objection to the specification for being confusing as two sequences are described by SEQ ID NO:29 in the amendment filed July 27, 2004. In addition, the sequence listing and computer readable form only provides 21 sequences. Clarification is needed.

Correction of the above and compliance with the sequence rules is required.

Drawing

6. The drawings are objected to because the label on each drawing, for example "Fig 1" or "Fig. 1A" is very small, all four figures need to have the same correction made. Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the

remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Sequence Compliance

7. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR1.821 through 1.825; applicant's attention is directed to the final rule making notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). To be in compliance, applicant is required to identify all amino acid sequences of at least 4 L-amino acids and at least 10 nucleotides by a sequence identifier, i.e., "SEQ ID NO:". The sequence listing paper copy filed on April 5, 2004 and the computer readable form filed on July 27, 2004 indicate that there are 21 sequences in the instant application, however, the specification discloses sequences such as SEQ ID NO:24 which indicates that sequences are not reported in the paper copy and computer readable form that are encompassed in the application. As these sequences have not been disclosed in the computer readable form of the sequence listing and the paper copy thereof, applicant must provide a computer readable form of the "Sequence Listing" including these sequences, a paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification, and a statement that the content of the paper and computer readable form copies are the same and,

where applicable, include no new matter as required by 37 CFR 1.821(e) or 1.821(f) or 1.821(g) or 1.821(b) or 1.825(d). See the attached Notice to Comply with the sequence rules.

Withdrawn-Claim Rejections - 35 USC ∋ 112

8. Previous rejections to claims 31-32 under 35 U.S.C. 112, second paragraph is withdrawn because a search of the term "uncommon fatty acids" indicate that this is a term of the art.

Maintained and New - Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 30-32 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 30-32 are drawn to methods of using transgenic cells having a nucleotide sequence that encodes an enzyme that is claimed solely by function and without any structural limitations. The claims are directed to a genus of nucleotides that are not adequately described

as a skilled artisan cannot envision the detailed chemical structure of the fragments encompassed in the claims. The Court of Appeals for the Federal Circuit has recently held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as be structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials'. University of California v. Eli Lilly and Co., 1997 U.S. App. LEXIS 18221, at *23, quoting Fiers v. Revel, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original). To fully describe a genus of genetic material, which is a chemical compound, applicants must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus and (2) identify the common characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these. In the instant specification, a novel enzyme activity is described as a phospholipids: diacylglycerol transferase (PDAT). Some plants, and not others, have this activity (see page 16 of the instant specification). A yeast gene, YNR008w, was tested for this activity and was confirmed to be a PDAT that can be over expressed in yeast and *A. thaliana* to increase fatty acid content in cells. The specification also describes numerous shorter DNA's and encoded proteins putatively described as PDAT genes; however, no testing on these gene fragments has been preformed to confirm the proposed function. Thus, one species of the claimed genus has been fully described, that is the use of the S. cerevisiae sequence (SEQ ID NOs: 1 and 2) to produce transgenic organism with increased triacylglycerol production. The specification fails to provide any additional representative species of the claimed genus to show that applicant was in possession of the claimed genus. A

representative number of species means that the species, which are adequately described, are representative of the entire genus. The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, disclosure of drawings, or by disclosure of relevant identifying characteristics, for example, structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. Further, no relationship between the disclosed species and the structures of the other proposed species is described. No common characteristics, other than the enzyme function, is required in the claims. Thus, one of skill in the art would be unable to predict the structure of other members of this genus based on the instant disclosure. Therefore, for all these reasons the specification lacks adequate written description, and one of skill in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

10. Claims 30-32 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of making triacylglycerol using a host organism transformed with a gene encoding PDAT from *S. cerevisiae* (SEQ ID NO:1), does not reasonably provide enablement for methods using any gene encoding any PDAT from any source absent any structural limitations. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. The enablement requirement refers to the requirement that the

specification describe how to make and how to use the invention. There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue. These factors include, but are not limited to: Quantity of Experimentation Necessary; Amount of direction or guidance presented; Presence or absence of working examples; Nature of the Invention; State of the prior art and Relative skill of those in the art; Predictability or unpredictability of the art and Breadth of the claims (see *In re Wands, 858 F.2d at 737, 8 USPQ2d at1404 (Fed. Cir. 1988)*. The factors most relevant to the instant invention are discussed below. To find additional PDAT genes and use them in the claimed methods would require undue experimentation.

In the instant specification, a novel enzyme activity is described as phospholipids: diacylglycerol transferase (PDAT). Some plants, and not others, have this activity (see page 16 of the instant specification). A yeast gene, YNR008w, was tested for this activity and was confirmed to be a PDAT that can be over expressed in yeast and *A. thaliana* to increase fatty acid content in cells. The specification also describes numerous shorter DNA's and encoded proteins putatively described as PDAT genes; however, no testing on these gene fragments has been performed to confirm this function.

The instant specification proposes 5 additional species of PDAT genes (6 total) and provides guidance and working examples to test for their activity. However, the nature of the invention is that genes encoding PDAT must be known to practice the claimed invention; the prior art provides none of these with respect to structure and related function. Due to the lack of a structure/function correlation analysis of the yeast PDAT gene, proven to function as a PDAT

in the instant specification, it is wholly unpredictable which of the disclosed fragments of yeast and plant sequences encode additional PDATs. Moreover, the full-length sequences are not disclosed; only ESTs are disclosed. While a skilled artisan could find additional full length sequences using the disclosed ESTs and functional assays, the ability to find does not fulfill the statutory requirement of the ability to make. Having the instant disclosure in full view of the prior art, one of skill in the art would be unable to predict the structure of PDAT genes so as to be able to make them, even in the likeness of SEQ ID No:1 (the *S. cerevisiae* sequence).

Additionally, the claims are not enabled for methods to produce triacylglycerol with uncommon fatty acids in organisms without the ability to natively produce triacylglycerol with uncommon fatty acids. To make some cells that produce TAG with uncommon fatty acids would require undue experimentation absent adequate guidance. Page 1 of the instant specification describes the claimed invention as being able to produce uncommon fatty acids "in combination with a gene for the synthesis of an uncommon fatty acid"; the PDAT gene does not regulate this process. Thus, to effectively practice the claimed methods, one would be required to use organisms that naturally produce uncommon fatty acids or to use organisms also transformed with a gene for the synthesis of an uncommon fatty acid. The specification provides no guidance or working examples for producing uncommon fatty acids in the absence of uncommon fatty acid genes (either endogenous or exogenous).

Moreover, the claims are directed to a method to produce host cells with increased overall oil content and the instant specification is not enabled for said method. The specification describes methods that increase the fatty acid content of host cells wherein a PDAT gene is over-expressed (see page 19, and Table 2), however, the specification does not describe increasing

the overall oil content of the host organism, which is a distinct method. As noted in WO 96/38573 on page 1, "[c]urrently, there are no documented demonstrations of increase in oil content by transgenic means...[i]n contrast, increased in the proportions of some strategic fatty acids have been achieved by the introduction of various plant fatty acid biosynthesis and acyltransferase genes in oilseeds". The state of the art provides no examples to support the scope of the claimed invention.

Thus, for all these reasons, the specification is not considered to be enabling for one skilled in the art to make and use the claimed invention as the amount of experimentation required is undue, due to the broad scope of the claims, the lack of guidance and working examples provided in the specification and the high degree of unpredictability as evidenced by the state of the prior art. Further, attempting to find additional PDAT genes and use them in the claimed methods or to make some cells that produce TAG with uncommon fatty acids or a construct a method to produce host cells with increased overall oil content would constitute undue experimentation absent adequate guidance in the specification. Therefore, applicants have not provided sufficient guidance to enable one of skill in the art to make and use the claimed invention in a manner that reasonably correlates with the scope of the claims, to be considered enabling.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

11. Claims 30-32 remain rejected under 35 U.S.C. 112, second paragraph, as failing to set forth the subject matter, which applicant (s) regard as their invention.

Claim 30 remains indefinite for equating "a nucleotide sequence" with "a DNA encoding" as this lacks parallel construction; both should recite either nucleotide or DNA for clarity, one term not both (see also claims 31 and 32 where the same language appears). The claim is also unclear following the "whereby" clause because it is unclear if the phrases that follow are meant to further limit the nucleotide sequence contained in the transgenic cell or organism? If so, the claim should read, "whereby said nucleotide sequence". In addition, does the phrase beginning "in which" mean to define a function of the nucleotide sequence (or DNA)? Further, the phrase "in which the said enzyme" represents improper English, it is suggested that "the" is deleted from the phrase.

Claim 31 is indefinite, because it is unclear if the recited "altered" is "an increased in oil content of the cell or organism". In addition, there is no indication of how much of an increase is attained.

Response to Applicant's Arguments:

12. Applicant's arguments have been fully considered but are not deemed persuasive for the following reasons. Note that the objections of record remain. The response on page 2+ state that "applicants believe all of the examiner's formal objections were overcome by the last filed response or are improper and overly restrictive as lacking support in the rules. This statement does not adequately address the issue raised as no amendment was provided to correct the

deficiencies or arguments to indicate why applicant believe the objections are improper as set forth in the Final rejection. As such the objections remain for the reasons stated above. The rejections under 35 U.S.C. 112, first and second paragraph, remain. Regarding the rejection under 35 U.S.C. 112, first paragraph enablement, the claims have been amended to recite "at least 95% sequence identity", in lieu of "such as 95% sequence identity". However, this amendment does not obviate the rejection of record. Additionally, the response filed on September 9, 2005 did not address this ground of rejection, thus the rejection remains. Moreover, The art generally recognizes that the structure of a protein is critical to its structure-function relationship and that a single amino acid change can have adverse effects on the protein's function. The instant specification does not provide sufficient guidance as to where in the structure changes will occur, what regions are conserved or demonstrate that the structure can tolerate modifications. The issue at hand is the breath of the claims in light of the predictability of the art as determined by the number of working examples, the skill level artisan and the guidance presented in the instant specification and the prior art of record. This make and test position is inconsistent with the decisions of *In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970)* where it is stated that "...scope of claims must bear a reasonable correlation to scope of enablement provided by the specification to persons of ordinary skill in the art...". Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily and improperly extensive and undue. See *In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988)*.

On page 2 of the response applicant states that the narrowing of the claim scope 95% homologous sequences should over come the Examiner's rejection under 35 U.S.C. 112, first paragraph written description. This assumption is not correct as the rejection has set forth that the enzyme is new, thus applicant needs to provide adequate written description pertaining to the fragments encompassed in the claims (large variable genus). While the specification describes SEQ ID NO:1 and anything encoding SEQ ID NO:2, as well as related sequences encoding proteins having the same PDAT function, the specification does not describe related sequences, such as within the 95% identity, having function. Thus, for all the above reasons, the instant rejection is maintained as amended herein.

Regarding the rejection under 35 U.S.C. 112, second paragraph, claim 30 remains indefinite based on equating nucleotide sequence with DNA and the whereby clause. Applicant on page 4 state that one of skill in the art would recognize the language of the claim as being definite. This argument is not persuasive for the reasons set forth above and because applicant sets forth no clear arguments as to why the phrases are not indefinite. Note that a new ground of rejection has been instituted under the same statute for the reasons set forth above. Thus, the rejection remains.

Maintained - Claim Rejections - 35 U.S.C. § 102

13. Previous rejection of claim 30 under 35 U.S.C. § 102(b) as being anticipated by Yu et al. as evidenced by Dahlqvist et al. is maintained for the reasons stated on the record. In addition, as the response filed on September 9, 2005 did not address the issues raised the rejection remains.

Withdrawn - Claim Rejections - 35 U.S.C. § 103

14. Previous rejection of the claims under 35 U.S.C. § 103(a) as being obvious over Verhasselt et al. taken with Zou et al. is withdrawn by virtue of applicant's arguments presented on pages 3-4 of the response filed September 9, 2005.

Conclusion

15. No claims are presently allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hope A. Robinson whose telephone number is 571-272-0957. The examiner can normally be reached on Monday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr, can be reached at (571) 272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Hope Robinson
Primary Examiner 11/21/05
Art Unit 1656

HOPE ROBINSON
PATENT EXAMINER